Neural Stem Cells Improve the Delivery of Oncolytic Chimeric Orthopoxvirus in a Metastatic Ovarian Cancer Model.

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Public Summary:
Oncolytic virotherapy offers a highly promising approach for treating ovarian cancer. Once seeded into the tumor, the oncolytic virus can selectively replicate in tumor cells (not in normal tissue) to destroy tumor cells. Each dying tumor cell then releases additional viral particles that infect neighboring tumor cells, spreading through the tumor until normal tissue is reached and viral replication stops. Importantly, oncolytic viruses can induce cancer cell death irrespective of radio- or chemoresistance, and can also stimulate immune recognition of cancer cells. Although clinical trials to date have demonstrated the safety of oncolytic viruses, the efficacy of this approach has been limited by delivery hurdles. The use of neural stem cells (NSCs) to deliver tumor specific oncolytic virus offers an unprecedented opportunity for effective viral distribution at multiple brain tumor sites. Here we demonstrate the potential of NSCs to deliver an oncolytic pox virus, a species that may be particularly potent against ovarian cancer. While this initial research still requires more development, this study provides a proof-of-principle demonstration that an NSC-mediated delivery of pox viruses can enhance the initial distribution of therapeutic viruses to ovarian cancer metastases.

Scientific Abstract:
Oncolytic virotherapy represents a promising approach for treating recurrent and/or drug-resistant ovarian cancer. However, its successful application in the clinic has been hampered by rapid immune-mediated clearance, which reduces viral delivery to the tumor. Patient-derived mesenchymal stem cells that home to tumors have been used as viral delivery tools, but variability associated with autologous cell isolations limits the clinical applicability of this approach. We previously developed an allogeneic, clonal neural stem cell (NSC) line (HB1.F3.CD21) that can be used to deliver viral cargo. Here, we demonstrate that this NSC line can improve the delivery of a thymidine kinase gene-deficient conditionally replication-competent orthopoxvirus, CF33, in a preclinical cisplatin-resistant peritoneal ovarian metastases model. Overall, our findings provide the basis for using off-the-shelf allogeneic cell-based delivery platforms for oncolytic viruses, thus providing a more efficient delivery alternative compared with the free virus administration approach.